

### REMARKS

Claims 1-6, 10-25 and 30-32 are active. Claims 1, 23 and 24 have been revised to further structurally characterize an activated pyrrole “that is an activated ester of pyrrole or a maleimide pyrrole”. Support for this limitation is found in the paragraph bridging pages 10-11 of the specification (or paragraph [0042] of the published application). New claims 30-32, which describe a structurally defined subclass of activated pyrroles, find support in Example 1B on pages 14-16 of the specification. Accordingly, the Applicants do not believe that any new matter has been introduced. Favorable consideration of this amendment and allowance of the application are respectfully requested.

### Interview Summary Record

On August 19, 2010 Examiner Haq and the Applicants’ representative reviewed the rejections set forth in the final rejection and discussed possible ways to overcome them. The term “activated pyrrole” was construed by the Examiner as encompassing an oligoT containing molecule of Livache, et al. and thus the term “coupling. . .directly to a protein” in claim 1 as not excluding this compound. It was suggested that the activated pyrrole be further structurally characterized, for example, by imposing the structural limitations of claim 22 on claim 1 to exclude the prior art oligoT compound. The Applicants were also encouraged to explain why the thickness of the copolymer film was not achieved by mere optimization in view of Table 3 or other experimental data.

### Rejection—35 U.S.C. §112, first paragraph

Claims 26-29 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. This rejection is moot in view of the cancellation of these claims.

Rejection—35 U.S.C. §103(a)

Claims 1-3, 6, 10-21 and 23-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Livache, et al., Biosens. Bioelec. 13:629, in view of Guedon, et al., Anal. Chem. 72: 6003. Independent claims 1, 23 and 24 have been revised to further structurally characterize the activated pyrrole and avoid the oligoT-containing compound of Livache, et al. which does not disclose a process according to these claims.

Rather Livache describes a process for preparing biochips by synthesizing a copolymer starting from a peptide substituted by an dT<sub>10</sub> oligonucleotide linked to a pyrrole and a pyrrole solution. Livache does not disclose or suggest an activated ester of pyrrole or a maleimide pyrrole.

Moreover, the combination of Livache with Guedon, which discloses DNA sensors and not protein sensors, does not suggest or provide a reasonable expectation of success for the subject matter of the present invention.

As previously pointed out, Livache which was applied in both obviousness rejections does not disclose a process as defined in the present application. Instead, Livache discloses a process for preparing biochips by synthesizing a copolymer starting from a peptide substituted by a dT<sub>10</sub> oligonucleotide linked to a pyrrole with a pyrrole solution. Thus, in Livache, the peptide is not directly attached to a pyrrole because an additional specific oligonucleotide is interposed between the two molecular moieties, i.e., between the peptide and the pyrrole. This is completely different than the structural configuration required by the invention.

Guedon, which was applied as a secondary reference in both obviousness rejections, discloses **DNA** sensors and not **protein** sensors (see title) and does not suggest or enable the

production of the subject matter of the invention which requires attachment of a protein to a conductive support.

Guedon discloses the hybridization signal obtained by these **DNA** sensors (not protein sensors) in view of the pyrrole film thickness. Those of ordinary skill in the art would have recognized the structural and functional differences between nucleic acids and proteins and chemical and biological differences between how these compounds interact with their ligands. Thus, one of ordinary skill in the art would not have equated the results obtained by Guedon for DNA with any expectation of similar results for protein sensors.

Nevertheless, assuming *arguendo* that DNA and proteins had identical properties, Guedon still teaches away from the thickness of 10 nm or less required by claims 19, 23 and 24. Guedon indicates that thicknesses of 9 nm to 14 nm were tested and the optimal hybridization signal was obtained for an 11 nm thickness. Based on this argument, one of ordinary skill in the art would have chosen a thickness of *more than or equal to 11 nm*, not one with a thickness of *10 nm or less* as required by claims 19, 23 and 24. Indeed, for a 11 nm thickness, the reflectivity variation is 0.90% and this variation stays above 0.60% for all samples having thicknesses above 11 nm, while it diminishes in a far more important way for samples having thicknesses less than 11 nm, see e.g., the reflectivity variation around 0.40% for a sample having a thickness around 9 nm. Thus, Guedon is non-analogous art since it refers to DNA and not to protein sensors, teaches no results-effective variable for optimizing the thickness of a pyrrole protein film according to the invention, and also teaches away from the invention should DNA and proteins be improperly equated as similar chemical molecules. Neither of these documents suggests that performance of the steps required by the invention would produce a superior more functional attached protein. Accordingly, for the reasons of record as well as in view of the remarks above the obviousness rejections based on Livache and Guedon cannot be sustained.

Response to Examiner's Arguments on pages 10-11 of the OA.

On page 10, first three paragraphs, the Examiner urges that the term “activated pyrrole monomer” is not clearly defined so as to exclude the Livache oligoT-containing compound. Claims 1, 23 and 24 have now been amended to require “an activated pyrrole monomer that is an activated ester of pyrrole or a maleimide pyrrole”. Livache does not disclose or suggest such activated pyrrole monomers.

In paragraph bridging pages 10-11 and on page 11 of the OA, the Examiner urges that the secondary reference, Guedon, is analogous art because both DNA and protein are “widely known analytes/probes useful for detection/analysis of biomolecules” (lines 9-11, page 11) and that one of ordinary skill in the art would recognize that DNA or protein could be substituted for one another depending on the analyte to be detected. However, while it is true that both DNA and proteins can be used to detect specific analytes, Guedon cannot provide a reasonable expectation of success for the superior properties obtained by the invention which pertain to protein interactions and not interactions between DNA molecules.

Furthermore, while the Examiner points to Guedon as disclosing a film thickness of DNA of 11 nm, this value falls outside the range required by claims 15, 19, 23 and 24 which require thickness of 10 nm or less. Moreover, the Examiner has not cited any prior art that establishes that a protein film having the thickness of the Guedon DNA film (11 nm) would have optimal or even good properties in view of the known differences between how DNA and proteins interact with their ligands.

On page 12, lines 5 *ff.* of the OA, the Examiner asserts that the thickness of no more than 10 nm required by the claims 15, 19, 23 and 24 could have been obtained by routine optimization. However, this argument ignores the differences between the prior art methods and those of the invention which require “coupling an activated pyrrole monomer that is an activated ester of pyrrole or a maleimide pyrrole directly to a protein to be attached to said

conductive support to obtain a first solution of a protein-pyrrole coupling compound". The prior art cannot disclose how to optimize such a coupling because it did not teach the activated pyrrole monomer of the invention.

Moreover, the prior art did not provide a reasonable expectation of success or disclose any results-effective variable for conserving the activity of a protein (e.g., its ability to interact with large molecules like antibodies) as described on pages 9 and 10 of the specification.

Rejection—35 U.S.C. §103(a)

Claims 4, 5 and 22 were rejected under 35 U.S.C. §103(a) as being unpatentable Livache, et al., Biosens. Bioelec. 13:629, in view of Guedon, et al., Anal. Chem. 72: 6003, and further in view of either in view of Domb, U.S. 2006/0013850 or Caillat, et al., U.S. Patent No. 6,803,228.

Livache and Guedon are distinguished above and did not suggest or provide a reasonable expectation of success for the invention.

Domb was relied on for teaching reactions between various chemical substrates and pyrroles, but did not suggest the process steps required by the present claims or provide a reasonable expectation of success for the superior functionality of proteins attached by these steps.

Caillat was cited as teaching a pyrrole polymer functionalized with N-hydroxysuccinimide and maleimide, but does not suggest the other aspects of the invention or provide a reasonable expectation of success for the superior functionality of the invention. Even if attachment of proteins to pyrroles is taught by the cited prior art, there is no suggestion of the results effective variables for obtaining the superior more functional

attached proteins of the invention by selecting the conditions discovered by the inventors.

Accordingly, this rejection may be withdrawn for the reasons discussed above.

CONCLUSION

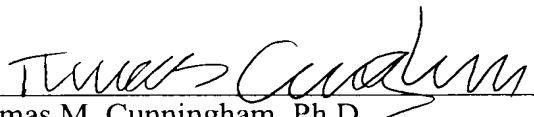
In view of the above amendments and remarks, the Applicants respectfully submit that this application is ready for allowance. Early notification of such is earnestly requested.

Respectfully submitted,

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